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Circular Letters:

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Frostbite: Physiology. When a limb is exposed to cold air at temperatures of 0° C. or lower, first it often, although not always, blanches, then with continued exposure regularly turns an intense pink color, and with further cooling, reverts to a cadaverous blanching. This white color persists for some time after the cessation of cooling, depending on the length and severity of the exposure. The next phase, during thawing or warming up, is invariably characterized by an intense red color, a rapid swelling, and a rise in the temperature of the limb. Blisters, which are usually present, grow rapidly and may burst within from 24 to 48 hours. The fluid is straw colored or sometimes blood tinged. If the blister persists for more than 24 hours, it is usually found to contain a dense gelatinous mass, which adheres to the underlying deep-red base. The tissue, especially in the areas of direct exposure, loses all sensation to pinprick, heat and cold, although pressure is usually perceived fairly well, probably because of transmission to adjacent healthy tissues. Within from 3 to 10 days, depending on the severity of exposure and individual predisposition, dry, dark-black areas may appear, followed by full-blown, demarcated, dry gangrene.

Fluorescein tests, performed during such a course of events, illustrate the pathologic physiology in the exposed tissue. Fluorescein, when injected intravenously, travels with the blood stream and, owing to its small molecule and its negligible electric charge, diffuses rapidly through the capillary walls. It can be detected wherever it is present by the intense golden-green light that it emits when activated by long-wave ultraviolet light in a dark room. The degree of fluorescence of an area is dependent mainly on the volume of blood reaching the area and on the capillary permeability. After intravenous injection of the dye an even slightly inflamed area will show an intense, golden-green fluorescence, which is in contrast to the pale-green appearance of normal tissue.

A limb of an experimental animal (rabbit) exposed to intense cold by immersion in alcohol at -30° C. for thirty minutes shows a complete absence of fluorescence during, and for approximately an hour after, the exposure. Slowly thereafter the dye starts to reappear in the previously cooled area, and within four hours a repeat fluorescein test reveals a marked hyperfluorescence due to the increased blood flow and to the increase in the permeability of the damaged capillaries. Pressure with a glass spatula on such an area reveals a persistent hyperfluorescence, indicating that the increased amount of dye is in the interstitial space and not only in the blood vessels. In a normal light, marked swelling and reddening of the limb are seen to be present. The limb is hot and the pulse is bounding. Under the capillary microscope the capillaries show marked dilatation and rapid flow. A fluorescein test, repeated from 48 to 144 hours later, reveals that the exposed region is again completely nonfluorescent and indicates vascular occlusion with impending gangrene. The same sequence of events can be observed in severe frostbite in human beings.

If the tissues exposed to cold are observed with a capillary microscope just before freezing occurs, the red cells are seen to gather into irregular clumps or

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masses, with plasma in between. Immediately after thawing, when the flow
starts again, the cells gradually resume their discreteness. This apparently
has no relation to the subsequent formation of occlusive red-cell masses due
to excessive transudation of fluid through the hyperpermeable capillary walls.

Pathology. Microscopical studies during the phase of increased blood flow
reveal that, apparently owing to the fluid loss caused by the increased capillary
permeability, the red cells start to silt up the capillaries, forming sludge that
contains some platelets but little fibrin. These occlusive red-cell masses are
not true fibrin thrombi but should be called "agglutinative thrombi." From 3 to
8 days after exposure these agglutinative thrombi start to undergo hyalinization,
and develop into completely hyalinized occlusive masses.

It is interesting to note that, in accordance with the observation of Siegmund
the protein content of all blisters examined while still in the liquid state was al-
most identical with the plasma protein content of the subject. Within from 24 to
48 hours a dense fibrin clot was formed in every blister. It may be assumed
that the same process takes place in the interstitial space and thus gives rise
to the subsequent fibrosis and collagenous deposition noted in histologic sections,
a process described by Rémy and Thérèse as "lardaceous inflammation." Many
lymphatic vessels also show clogging with fibrin deposition. All this can be at-
tributed to the tremendously increased capillary permeability.

Therapy. Since the gangrene subsequent to frostbite is due to the occlusive
red-cell sludge in the capillaries, and since some of the damage to muscles and
nerves seems to be due to interstitial fibrin deposition leading to fibrosis, it ap-
peared interesting to determine whether heparinization would interrupt the chain
of events.

Twenty-one rabbits, exposed to cold by immersion of one of their hind legs
in alcohol at -30° C. for 30 minutes, were heparinized intravenously for 5 or 6
days after exposure, the clotting time (Lee-White method) being kept between
30 and 60 minutes. Eighteen of the animals escaped gangrene completely, where-
as 3 showed some surface lesions without loss of the limb. Twenty control ani-
mals, exposed in the same way but not heparinized, lost their legs by complete
gangrene, including the bone. These animals showed dry gangrene with spontane-
ous amputation. Except for sterile dressings no surgical intervention was
necessary in any of the animals. These findings, together with experience in 14
human patients with frostbite, treated before the introduction of heparin therapy,
convinced the authors that an extremely conservative approach is indicated in re-
gard to amputations. Self-demarcation and the astounding recuperative power of
frostbitten tissue force one to assume an attitude entirely different from that in
cases of gangrene due to arteriosclerotic vascular disease. Histologic examina-
tions of the exposed legs of the heparinized animals reveal that the red-cell con-
glomerates, regularly found in all smaller vessels of nonheparinized exposed ani-
mals, are missing. The vessels are found empty or with a normal content of cell
and plasma. Since swelling and increased permeability, as evidenced by fluores-
cein tests, are observed to the same extent in heparinized as in untreated animal

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it must be assumed that the increased permeability leads to the accumulation of the red cells by stranding but that they cannot stick together if heparin is present in the blood stream.

In 4 of a group of 8 volunteers who were undergoing treatment for sub-acute bacterial endocarditis, frostbite was accomplished by means of a porcelain crucible filled with dry ice and applied without pressure to the skin of the lateral aspect of the upper arm for ten minutes. An area about 2 cm. in diameter came in contact with the skin, which attained a temperature of about -22° C. Heparinization was started immediately after exposure. One volunteer served as a control. The others were subjected to local refrigeration in the same manner but for 2 exposures of 30 minutes each. The initial or control exposure was permitted to develop for 6 days before the second frostbite was induced, immediately followed by subcutaneous injection of heparin in Pitkin menstruum. The clotting time in the treated subjects was kept between 25 and 60 minutes. The tissue associated with the lesions that were followed by adequate treatment escaped deeper injuries whereas central necrosis approximately 1 cm. in diameter and from 3 to 5 mm. in depth developed in the control lesions.

A second group of 4 volunteers was subjected to freezing of an area 3.5 cm. in diameter for 30 minutes by means of beakers filled with dry ice. Each volunteer received at least four exposures, and (1) no treatment, (2) immediate heparinization for 6 days subsequent to exposure, (3) heparinization for 6 days after an initial delay of 24 hours, and (4) heparinization for 6 days after an initial delay of 24 hours during which the exposed part was kept cool by means of an icebag applied to the lesion without pressure.

The results were similar in all the volunteers. With no treatment, gangrene developed. Immediate heparinization lasting 6 days prevented gangrene. Heparinization after a 24-hour delay at room temperature gave almost as good a result as immediate heparinization. Cooling in the interim produced the poorest results. Blister formation, which takes place rapidly in all exposed areas, is prevented in lesions kept cool after exposure. Immediately after the ice bag has been removed, however, the blisters arise rapidly and are even larger than those in the control lesions. This delay in the appearance of the blister may have led to the belief that cooling after exposure to low temperatures is beneficial.

The blister content in all heparinized patients stayed liquid throughout. No clot formation was noticed. If the blister did not rupture in the initial phase of marked tension its content was slowly resorbed, a loose shriveled piece of skin remaining on the exposed spot. The fact that heparinization keeps the interstitial fluid, with all its constituents, resorbable is of importance in the prevention of subsequent fibrosis and collagen replacement.

A third group of 3 volunteers was subjected to freezing of an area 5 cm. in diameter by means of a metal capsule kept at -30° C. for thirty minutes. Each volunteer received at least five exposures with the consecutive lesions followed

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by (1) no treatment, (2) warming for 24 hours after exposure but no heparinization, (3) immediate heparinization for 7 days, (4) heparinization for 7 days after an initial delay of 24 hours, and (5) heparinization for 7 days after an initial delay of 24 hours during which the exposed part was warmed by an electric heating pad. The results were similar to those in the previous group. Exposure with no treatment led to gangrene, warming without heparinization made the gangrene more extensive, immediate heparinization prevented gangrene completely, and heparinization after twenty-four hours gave almost as good a result as immediate heparinization. Warming for 24 hours to 44° C. in the interval before heparinization produced a lesion that was almost as large as the untreated control lesion, although not so severe as the lesion with interval cooling in the previous group of volunteers. Although loss of tissue was completely prevented in the cases with early heparinization, all sensation was lost for at least 3 months. The same loss of sensation occurred in the treated animals with complete maintenance of tissue. The motor disturbances in these animals, as demonstrated by dragging of the leg, disappeared in from 4 to 6 weeks.

It was conspicuous in all the volunteers that the individual reaction to a standard exposure varied widely but was rather constant in the same subject. An exposure that consistently led to extensive gangrene of the entire exposed area in one volunteer failed to produce any tissue breakdown on repeated attempts in another. It may thus be possible to screen persons with an unusually high sensitivity to cold by means of standard test procedures.

The heparinization in the last two groups and in the following cases was carried out by intravenous drip. Approximately 300 mg. of heparin in 2000 c.c. of physiologic saline solution per 24 hours was given approximately at the rate of from 20 to 25 drops per minute. The clotting time (Lee-White method) was kept between 30 and 60 minutes and was checked every 12 hours. No untoward effects were seen in any of the persons treated by this method. Whenever possible, a vein on the middle part of the extensor surface of the forearm was used for the administration of the intravenous drip. The needle and a wide loop of the connecting tubing were fixed to the forearm by adhesive tape. No splint was used at any time, nor in any case was it necessary to insert the needle more than twice.

In two actual cases of severe frostbite this method of treatment was used. One patient had been exposed to a temperature of from 12 to 13° F. for 8 hours while lying with bare hands motionless on the pavement. The other had been exposed to a temperature between 14 and 18° F. for 12 hours while lying motionless with bare hands on the pavement. Both patients had severe degrees of hemorrhagic blistering within 24 hours of exposure. Heparinization was started 6 and 10 hours respectively after the exposures and carried out according to the method mentioned above for 7 and 5 days respectively. The hands were dressed under sterile conditions, since frostbitten tissues seem extremely susceptible to infection. Precautions similar to those employed in the treatment of burns were used, and wet penicillin dressings (1000 units per cubic centimeter) were applied to the

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blistered and denuded areas. Both patients escaped any loss of tissue except for the loss of the nails. Although it cannot be stated with certainty that without treatment gangrene would have ensued, there is good reason to assume from previous experience that this would have occurred. (New England J. Med., 11 Sept. '47 - K. Lange et al.)

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Gold Therapy in Rheumatoid Arthritis: Treatment of rheumatoid arthritis with gold compounds, initiated in Europe twenty years ago, has gradually grown in favor in American medicine during the past ten years. Recently, Fraser condensed the literature on chrysotherapy in this disease and noted that most observers report a favorable response in from 70 to 80 per cent of patients. Short, Beckman, and Bauer found more than forty publications on gold therapy in the English literature up to 1946, almost all of which were favorable toward this type of treatment. When that report appeared, the authors were engaged in reviewing six years' experience with gold treatment in the Arthritis Clinic, Indianapolis City Hospital.

In this survey, the records of 52 patients treated with gold were examined. Five of these were eliminated at the outset because the patients had received less than 100 mg. of gold salts. The records in the remaining cases form the basis for this report. All patients had a definite diagnosis of active rheumatoid arthritis. All were adults ranging in age from 20 to 64 years at the time treatment was begun. There were 34 women and 13 men, representing a sex ratio of a little less than 3:1. The longest period of observation was six years, but all patients were followed for more than eighteen months. The stage of disease at the time treatment was initiated varied from less than two years' duration in 18 cases, or 38 per cent, to the later stages of the disease in 29, or 62 per cent. Patients with more advanced involvement had been treated elsewhere with the usual variety of remedies, but none had previously been treated with gold.

All patients received gold therapy in amounts ranging from less than 500 to more than 3000 mg. of a salt containing 50 per cent gold. During the first years of chrysotherapy the customary weekly dose of 100 mg. of gold salts was given to a total of 1000 mg. per "course." Gold sodium thiomalate (Myochrysine) was the standard compound, although for about a year gold acetyl cystein was given. Since both compounds contain 50 per cent gold, they are considered comparable therapeutic agents. During the past four years, the current practice of giving lower weekly doses was followed, with most patients receiving 50 mg. of gold sodium thiomalate or 25 mg. of actual gold. The total amount per course has remained at 1000 mg. of the salt, but in most patients now under treatment, maintenance therapy of 25 mg. every two weeks has been continued indefinitely after a course has been completed. In addition, acetyl salicylic acid has been used freely to control pain, and application of heat to affected joints has been a daily routine with the majority of patients.

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In these patients treated with gold salts the results have not approached those reported in the majority of publications on this subject. The patients who continued in an improved state after treatment constituted only 23 per cent of the total, whereas 62 per cent showed no appreciable change, and 15 per cent became worse. It is interesting that 8 patients who were given only from 500 to 1000 mg. showed the greatest percentage improvement of any group, in fact, 17 per cent greater than that in the group of 10 patients who were given more than 3000 mg. The next greatest improvement was in the 9 patients who received less than 1500 mg. This suggests that the first course of gold is the most effective, a finding noted by others. It is interesting that 6 of the improved patients, 5 of those in the unchanged group, and all 7 listed as failures had been victims of the disease for less than two years. With these 18 patients as a group representing the earlier stages of rheumatoid arthritis, 33 per cent were improved, 28 per cent were unchanged, and 38 per cent became worse with gold therapy. A possible effect of gold in preventing advance of the disease may be implied concerning the 62 per cent (of the entire group) who showed no measurable change for better or for worse as a result of treatment. In 62 per cent of the patients toxic reactions to gold were noted. Although most of these side-effects were of little consequence, there were 2 cases of exfoliative dermatitis, with 1 death.

An explanation for the results in this series of cases may be found in the longer period during which these patients were observed. In many cases apparent improvement was seen after treatment, but in few cases was there a lasting effect. In this report no attempt was made to discuss separately patients who improved only to relapse, for it is believed that a period of more or less temporary relief is of little consequence in this disease.

The percentage of improvement in this series happens to be the same as the 23-percent net improvement reported by Short, Beckman, and Bauer in 35 cases. In contrast, through the use of general and orthopedic treatment, those authors obtained improvement in 52.9 per cent of a larger series of 274 cases without the risk that is always associated with gold therapy. (New England J. Med., 18 Sept. '47 - J. S. Browning et al.)

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Ambulatory Treatment of Hallux Valgus: Prolonged rigid splinting and restriction of walking activity for periods of from 2 to 6 weeks have constituted the routine of most orthopedic surgeons after operations for correction of hallux valgus. As a result of this prolonged immobilization without the functional stimulus of weight-bearing and walking, some permanent loss of motion in the metatarsal phalangeal joint has followed many of the operations. Hallux rigidus or hallux varus, which occasionally resulted, produced severe disability.

In addition to these complications, which may be relatively infrequent in the hands of experienced orthopedic surgeons, there is always greater cost and hence an economic objection to prolonged hospitalization made necessary by the

usual procedure of rigid splinting and non-weight-bearing for a period of several weeks.

Because facilities did not permit hospitalizing patients with hallux valgus who came to the Central Free Dispensary of Rush Medical College where the authors worked during 1940 and 1941, operation under local anesthesia followed by out-patient care was decided upon.

The block of the metatarsal phalangeal region was started at midfoot and a tourniquet applied around the foot at that level. The surgical technics used included the McBride, the Mayo, and the Silver operations with various modifications. The sesamoid bones were removed whenever they were found to be hypertrophied or their articular surfaces degenerated. Debridement of the joint was carried out when indicated. No rigid splint of any kind was used. In each instance the toe was held in a position of varus by corrective bandaging (see figure below). The blood which subsequently stained the dressing dried

and reinforced the bandage. Patients were permitted to walk from the operating room without assistance. Absence of pain because of the novocain anesthesia made it comparatively simple to persuade them to do this. Most of them had to go home by streetcar and some of them traveled long distances. The dressing was inspected the following week, but was not changed for two weeks after the operation.

A total of 24 patients were subjected to one or more operations for hallux valgus and then permitted to go home immediately by whatever transportation they could obtain. There were no complications. The results which were obtained were definitely better than those which had been observed in the authors' patients whose care had included from 2 to 3 weeks of hospitalization with complete immobilization. These patients suffered minimal pain and all of them returned to the clinic walking surprisingly well and with an excellent range of motion in the metatarsal phalangeal joint.

Encouraged by these results, since 1941 the authors performed 26 operations on 17 hospitalized private patients for hallux valgus and bunions. A general anesthetic was used in 6 cases because the patients refused to permit the use of a local anesthetic, or because other surgical procedures were also to be carried out. In

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11 cases 1-percent novocain was used as a local anesthetic. The patients who were operated upon under local anesthesia were encouraged to walk about their rooms immediately after the operation and were given bathroom privileges. Because of the persisting anesthesia, they experienced no pain. On the second and third day these patients did complain of some pain, but it was not sufficient to prevent them from bearing weight and walking.

The patients varied in ages from 23 to 75 years and their occupations were those in which at least an average amount of walking was necessary. They were discharged as recovered in from 4 to 8 weeks following surgery. There have been no complications or unfortunate sequelae.

The plan of postoperative care may be summarized as follows:

1.   The hallux should be splinted by means of corrective bandaging, without rigid fixation, following operation. Two 2-inch gauze bandages should be used for each foot. Multiple layers of bandage are essential if correction of the hallux valgus is to be maintained while ambulation is permitted.

2.   Walking with full weight-bearing is begun immediately after operation when a local anesthetic is used, and on the next day following general anesthesia.

3.   The patient may be discharged from the hospital from 2 to 4 days after operation.

4.   The original dressing should be changed and the stitches removed 14 days after operation.

5.   The functional splinting by corrective bandaging should be continued for an additional period of 2 weeks.

6.   Patients may be encouraged to resume their normal activities at the time that the bandaging is discontinued.

7.   After bandage splinting is discontinued, the foot should be soaked in warm, slightly soapy water for 20 minutes each day. While in the warm water the toe should be actively exercised.

8.   Low heel, soft leather oxford shoes with a stiff shank, straight inside last, and metatarsal pads should be worn for at least 3 months.
(Surgery, Sept. '47 - E. L. Compere and W. J. Schnute)

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Treatment of Acute Renal Insufficiency with Peritoneal Lavage: Acute renal failure and uremia occur in certain cases in which irreversible renal changes cannot be demonstrated. The mortality rate in such cases unfortunately is high because of the rapid and marked accumulation of nitrogenous and other

waste products. Many such patients might recover, if a means of eliminating toxic end products of metabolism, during the period of suppressed renal function, could be devised.

The peritoneum, which has a filtering surface of approximately 22,000 sq. cm. in the average adult, has long been recognized as an excellent dialyzing membrane. Ganter, in 1923, was the first to employ peritoneal lavage as a means of treating renal insufficiency, and a few reports of similar clinical trials have appeared in the literature since that time. Within the past year the excellent experimental and clinical reports of Fine, Frank, and Seligman have been largely responsible for an increasing interest among both physiologists and clinicians in acute temporary renal insufficiency. As far as could be ascertained, 27 cases of renal insufficiency in which peritoneal dialysis was attempted have been reported in the literature up to the present time. (Since this paper was written an additional case has been reported.) Of the 27, 9 patients had serious organic disease with advanced irreversible damage in the kidneys. Eight of these 9 died soon after peritoneal lavage was carried out and the fate of the ninth is unknown. The diagnosis is unknown in 3 cases in which the outcome was also reported as unsuccessful. In the 15 remaining cases, in which the diagnosis indicates possible reversible renal impairment, 8 recoveries (53 per cent) have been reported.

The authors have employed peritoneal dialysis in 2 cases of acute renal insufficiency. The method used in one case of carbon tetrachloride poisoning, which is reported upon in detail by C. C. Pearson in the same issue of the Proceedings of the Staff Meeting of the Mayo Clinic in which this report appears, was that described by Fine and his associates in the Annals of Surgery of November 1946. Modified Tyrode's solution was used with the addition of the sodium salt of heparin to inhibit the formation of fibrin on the peritoneum, and of penicillin to inhibit bacterial growth. Because of the patient's obvious tendency to bleed, only 0.25 mg. of heparin per liter was used, since it was not known to what degree heparin might be absorbed from the peritoneum into the circulation. Subsequent experience has shown that absorption of heparin when used in dosages up to 1 mg. per liter of dialysate is not sufficient to effect significantly the coagulation time of the blood. Penicillin was added to the dialysate in the dosage of 5,000 units per liter, and 30,000 units were given intramuscularly every 3 hours from the time the procedure was instituted. On the patient's sixth day in the hospital a positive culture for Pseudomonas aeruginosa, Aerobacter aerogenes, and a micrococcus was obtained from the peritoneal washings. On this day the amount of penicillin in the lavage fluid was increased from 5,000 to 10,000 units per liter and the intramuscular dose was increased to 50,000 units every 3 hours. Sulfadiazine was not added to the irrigating fluid because of the possibility of inflicting further injury on an already damaged pair of kidneys. The authors believe, however, that the addition of 0.1 Gm. of sulfadiazine per liter (1:10,000), an amount entirely adequate to inhibit growth of most Gram-negative organisms with the exception of P. aeruginosa, will not create any significant hazard of additional renal damage, particularly if the concentration of sulfadiazine in the blood is watched daily. The addition of

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streptomycin, when available, to the dialysate might be desirable.

The apparatus used by the authors differed from that previously described in that the bacterial filter was omitted (see figure below). This was done for
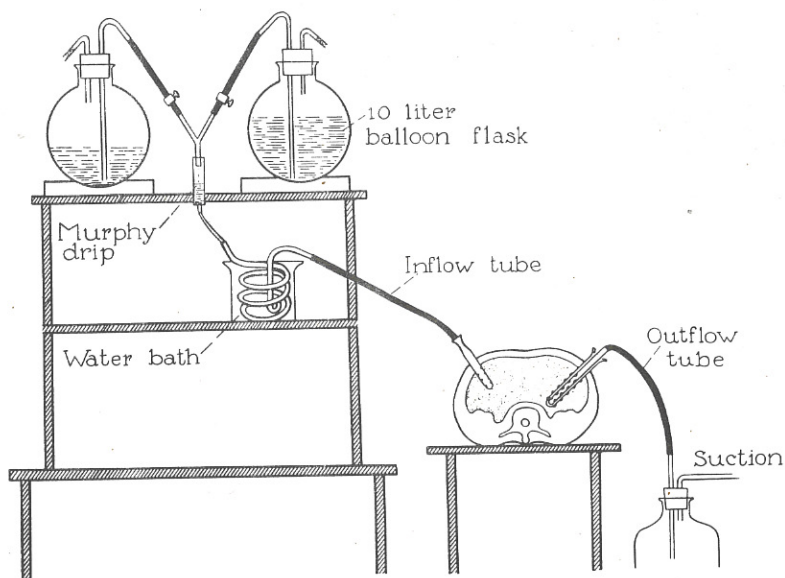
Apparatus used for peritoneal lavage.

three reasons: (1) such a filter materially interferes with maintenance of an adequate rate of flow of irrigating fluid into the peritoneal cavity; (2) after a period of one or 2 hours, organisms may grow through the filter into the circu-lating fluid on the distal side; and (3) the authors believe that bacteria are more likely to gain entry to the peritoneal cavity in and around the peritoneal tubes (especially the sump drain) rather than in the fluid itself. It is further possible that organisms may enter the peritoneal cavity in a retrograde manner from the nonsterile suction system employed to remove dialyzing fluid from the peritoneal cavity. The authors took strict precautions to keep the area about the peritoneal openings as aseptic as possible. Although lethal peritonitis did not occur in their two cases, the authors did culture Gram-negative organisms from the peritoneal washings, as was also reported for a number of the cases in the literature.

Seligman, Frank, and Fine have shown that the clearance of urea across the peritoneum is proportional to the flow of irrigating fluid through the peri-toneal cavity, the optimal rate of flow being from 30 to 50 c.c. per minute. Kolff stated that the optimal rate of flow is from 1,000 to 1,200 c.c. per hour (from 16 to 20 c.c. per minute). In this case of carbon tetrachloride poisoning, the patient complained bitterly of abdominal pain and nausea if the rate of flow was increased to more than 17 c.c. per minute.

The authors employed identical tubes (sump drains) for both inflow and outflow tubes (see figure on following page) except that the air holes at the shoulder of the inflow tube were obliterated. This modification makes it possible

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to reverse the direction of flow through the peritoneal cavity merely by interchanging the inner portions of the tubes, leaving the outer sheaths in place. Such a reversal of flow may be necessary from time to time in order to avoid omental interference and "channeling."

Peritoneal tubes (sump drains). The drain on the right with airflow holes obliterated is used for inflow.

Maintenance of normal electrolyte balance and the prevention of overhydration and dehydration have presented major difficulties in a number of cases in the literature and this case is not exceptional in this regard. In this patient, on the fifth day of dialysis some increase in the degree of peripheral edema was observed, and it was suspected that the patient might be absorbing fluid from the peritoneal cavity into the circulation. Accordingly, the molecular structure of the irrigating fluid was examined carefully. It was noted that in the formula being used the amount of chloride (145 mEq. per liter) was excessive in proportion to the amount of sodium (151 mEq. per liter) and bicarbonate (12 mEq. per liter). This suspicion was confirmed the following day when the concentration of plasma chlorides soared to 672 mg. per 100 c.c. (114.0 mEq. per liter) with a decrease in the carbon dioxide combining power to 41.9 volumes per cent (18.9 mEq. of bicarbonate per liter). Accordingly, the amount of sodium chloride used was decreased from 8 to 6 Gm. per liter and the amount of sodium bicarbonate was increased from 1 to 3 Gm. per liter (see table below). This correction resulted in a solution the milliequivalent structure of which more closely approximates that of normal blood plasma: chlorides, 109 mEq. per liter;

Composition of various solutions used for peritoneal dialysis

Solutes	Solution, gm. of solutes per 1,000 c.c.						
	Ringer's	Locke's	Tyrode's	Modified Tyrode's	Hartmann's	A*	P
Sodium chloride (NaCl)	9.0	9.0	9.0	8.0	6.0	6.1	6.0
Potassium chloride (KCl)	0.3	0.24	0.2	0.2	0.3	0.35	0.2
Calcium chloride (CaCl2)	0.25	0.42	0.2	0.1	0.2	0.23	0.1
Magnesium chloride (MgCl2)			0.1	0.1		0.05	0.1
Sodium acid phosphate (NaH2PO4)			0.05	0.05		0.07	0.05
Sodium bicarbonate (NaHCO3)	0.2	0.2	1.0	1.0		2.20	3.0
Sodium lactate (NaC3H5O3)					3.1		
Dextrose		1.0	1.0	1.5		10.0-20.0	20.0

*Abbott and Shea.

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sodium, 139 mEq. per liter; and bicarbonate, 36 mEq. per liter. In an attempt to correct the increasing edema, P solution was made hyperosmolar by increasing the dextrose content from 1.5 to 20 Gm. per liter. Correction of the patient's chloride acidosis and a noticeable decrease in the amount of peripheral edema were observed during the final three days of the patient's life.

The authors have employed successfully the P solution for peritoneal lavage in the other of the two cases mentioned (to be reported upon at a later date) and had little or no difficulty in maintaining correct electrolyte and fluid balance. They believe that Hartmann's solution and A solution, both of which are similar in composition to the P solution, may be employed with similar satisfactory results if they are made hyperosmolar by the addition of 2 per cent dextrose.

The authors believe further that if peritoneal infection can be kept under control, continuous irrigation should be maintained until the level of urea in the blood decreases to less than 100 mg. per 100 c.c., or until the amount of urine excreted in 24 hours approaches 1,000 c.c. with increasing concentrations of urinary urea or nonprotein nitrogen.

Peritoneal dialysis is a more or less formidable procedure and is attended by numerous risks and problems. For this reason, as a therapeutic measure, its use should be restricted to cases of acute renal failure associated with reversible renal changes. The risk of lethal peritonitis, though small, nevertheless remains a hazard. The problem of maintaining normal electrolyte and fluid balance is constantly present and the possibility of overhydration or dehydration must be constantly borne in mind. For these reasons, after acute urinary suppression with increasing renal insufficiency, 3 or 4 days of routine intravenous therapy and supportive measures should be employed in an attempt to promote excretion of urine. If at the end of this period, routine measures have failed and it appears that fatal termination may result, an attempt at extra-renal excretion by peritoneal dialysis should be initiated. (Proc. Staff Meet., Mayo Clin., 6 Aug. '47 - H. M. Odel and D. O. Ferris)

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<u>Thiouracils and Thioureas:</u> In the attempt to obtain antithyroid compounds which were superior to 2-thiouracil, it seemed important not only to test the thyroid-inhibiting effects of many related substances in animals but also to compare the activities of the more potent compounds in patients with thyrotoxicosis. Moreover, it was regarded as important to investigate the differences in the manner in which the body handles these drugs, especially as regards their absorption, distribution, destruction, and excretion. Studies of this nature have previously been made with thiouracil, thiourea, diethylthiourea, tetramethyl-thiourea and aminothiazole. All these drugs are rapidly absorbed from the gastro-intestinal tract and destroyed in the body. None of the first four compounds is excreted in the stools; approximately one third of these substances

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is excreted in the urine. In the case of thiouracil, which has been studied more extensively than the other compounds, the following significant observations have been made.

1. Accurate estimations can be made of its concentrations in all the tissues and fluids of the body.

2. It is rapidly absorbed from the gastro-intestinal tract, significant concentrations in the blood developing within fifteen minutes, but about 15 per cent of the drug is destroyed in the gastro-intestinal tract. The secretions of the stomach, duodenum and jejunum, but not the contents of the ileum, possess the capacity to break down the drug.

3. Most of the thiouracil in the blood is in the cells, and nearly all of it is bound to protein. It can be freed from the protein by digestion with trypsin; it has been released from serum by ultrafiltration at a low pH. The concentration of thiouracil in the blood rarely exceeds 6 mg. per 100 c.c., regardless of dosage, or renal or hepatic damage.

4. It has been found in essentially all the tissues and fluids of the body, but the concentrations have been different.

5. Approximately one half of the total amount of thiouracil ingested is broken down in the body, essentially all tissues possessing this capacity in varying degrees.

6. About one third of the drug ingested is excreted unchanged in the urine. The products of disintegration of thiouracil have not been established, but following its administration there is an increased excretion in the urine of neutral sulfur.

7. Thiouracil is transported through the placenta in biologically active quantities.

In the studies of other compounds related to thiouracil and reported upon in this paper not so many phases of action were investigated as were done with thiouracil, but certain comparative studies were made of thiothymine (5-methyl-thiouracil), ortho-phenylenethiourea and several thiouracils possessing hydrocarbon chains as substituents in the 6-position: methyl, ethyl, n-propyl, cyclopropyl, n-butyl, isobutyl, and amyl groups. The same method used in the determination of thiouracil was applied to these compounds.

The rate of breakdown of thiouracil was more rapid than of its derivatives with substituents in the 6-position: methyl, ethyl, propyl, butyl, or amyl. These derivatives accumulated in the body and thyroid gland of rats in much greater quantities than did thiouracil. Derivatives with an odd number of carbon atoms accumulated in the body in greatest amounts, but the largest concentrations in the thyroid gland occurred with derivatives bearing an even number of carbon

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atoms, namely, ethyl and butyl. In the case of all the compounds tested the concentration in the thyroid was many times greater than that in the body. There was no definite correlation of the amount of drug in the thyroid with its anti-thyroid activity.

In patients receiving more than 100 mg. of 6-propylthiouracil daily the con-centration of this compound in the blood was greater than that of thiouracil given in equivalent doses; there was no essential difference when the daily dosage was less than 100 mg. When either drug was given in doses of 50 mg. once daily, only a small amount was found in the blood after thirty minutes and none after two hours. Patients treated with 6-cyclopropylthiouracil were found to have a higher concentration in the blood than did those treated with 6-propylthiouracil or thiouracil. The concentration of ortho-phenylenethiourea was greater than that of the other compounds tested. Most of the 6-propylthiouracil and 6-cyclo-propylthiouracil in the blood, like thiouracil, exists in the cells. Roughly one third of the compounds was excreted in the urine.

Thiouracils combine with the proteins of the serum in varying degrees, but there does not seem to be any correlation of this reaction with the amount of antithyroid action.

Of the thiouracils studied, the derivatives accumulated in the body in greater concentration than did thiouracil. Moreover, the derivatives had a stronger antithyroid action than did the parent substance, but the antithyroid activity of the various compounds was not proportional to their concentration in the body or in the thyroid gland. In this connection, it should be pointed out that in a study of many patients treated with thiouracil there was no proportion-ate relationship of the content of thiouracil in the thyroid gland to the clinical response of the thyrotoxicosis. Furthermore, the concentration of thiouracils in the blood has not been associated with the amount of action in the thyroid gland. Therefore, the degree to which the compounds are stored in the thyroid is not the all-important factor in the determination of the amount of thyroid-inhibiting effect. Such factors as the intracellular distribution of the compound and the specific reactivity of the latter are doubtless of great significance. (Arch. Int. Med., July '47 - R. H. Williams and G. A. Kay)

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(Not Restricted)

<u>The Family and Dental Disease</u>: The present investigation is the fifth in a series of studies of the familial factors in dental disease and is concerned with the following specific question: Do children who drink fluoride waters all their lives and who have an average low rate of DMF (decayed, missing, and filled teeth) show a variation in caries susceptibility related to that shown by their parents?

In a preceding publication caries incidence in children was shown to be closely related to their parents' susceptibility. The now well-confirmed find-ing that the drinking of water containing small amounts of fluoride is associated

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with reduced caries attack rates leads logically to the question of whether an environmental factor, such as fluoride in drinking water, can overcome. and perhaps obscure, the more basic factor of familial susceptibility in dental disease.

For areas where fluorination of water supplies is contemplated or now under way, the findings of the present study are peculiarly pertinent since they are based on data concerning persons who had consumed fluoride waters in a certain area for 19 years. Accordingly, all children born in the area and not older than 19 years, who were permanent residents during the interval, were exposed to the waters all their lives.

From the data collected it was indicated that children with continuous exposure to fluoride water since birth are as a group protected against caries attack. However, the degree of protection varies among the exposed. Those who are protected least are children whose parents show the highest tendency toward dental disease, and those who are protected most are children whose parents show the lowest tendency to be attacked by dental disease. Exposure to an environmental factor (fluorine in the diet) will reduce the amount of caries attack, but not sufficiently to obscure the influence of the familial factor which may be constitutional in origin. (Pub. Health Reps., 29 Aug. '47 - H. Klein)

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(Not Restricted)

Wetting Agent for Contact Lenses: Although the present day plastic contact lenses are a great improvement over both the Mueller and the Zeiss glass contact lenses, there still are many problems that vex the ophthalmologist who prescribes and fits contact lenses. The most frequent complaint is fogging. The following are some of the more common causes for the fogging of vision experienced by the wearer of contact lenses: (1) improper refractive correction; (2) dirty contact lenses; (3) cloudy solution; (4) corneal edema; (5) spasm of accommodation; (6) clouding of the solution after insertion of lenses; and (7) meibomian-gland secretions on the anterior surface of the contact lenses. The first three causes for fogging can be eliminated by the ophthalmologist and the patient and are not discussed here.

Corneal edema usually comes on from 30 minutes to 4 or more hours after the insertion of the contact lenses. It is due to the imbibition of the buffer solution by the corneal epithelium. The continued daily wearing of the contact lenses seems to toughen the corneal epithelium so that as time passes the patient can wear the contact lenses for longer and longer periods of time before the fogging due to corneal edema begins. In some cases changing the strength or the formula of the buffer solutions will lengthen the time before fogging occurs.

Contact lenses, although well fitted, like any other foreign body in the conjunctival sac, induce stimuli which in turn produce undesirable reactions. Among these undesirable reactions is the spasm of accommodation noted in many cases,

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especially in the hyperopic patient when he first begins wearing contact lenses. This spasm of accommodation relaxes after a longer or shorter period of time as the eye becomes accustomed to the lenses.

In the same manner the contact lens acting as a foreign body stimulates the various paraocular glands. This at first thought would seem unimportant, but if it is recalled that the goblet cells are most numerous in the bulbar conjunctiva and that the scleral part of the contact lens acts as a funnel placed over the bulbar conjunctiva thus catching the mucus secreted by these glands, it can readily be seen how the stimulation of the goblet cells will cause the buffer solution to become cloudy due to the increased quantity of mucus. This, like the spasm of accommodation, decreases in most cases as the eye becomes accustomed to the presence of the contact lens.

The greasy secretion of the meibomian glands, essential as it is in preventing the tears from spilling over onto the cheeks and in sealing the eyelids during sleep, often proves to be the greatest problem with which the contact-lens wearer has to contend. In the first place, the manipulation of the eyelids during the process of inserting the contact lenses, massages the secretion from these glands; then the contact lenses by their presence in the conjunctival sac stimulate the meibomian glands, by reflex action, as well as the other paraocular glands, and an excessive amount of this special sebum is produced. This increased sebum on the lid margins would be of no consequence if the anterior surface of the contact lens were wet so that it would repel the greasy meibomian gland secretion. However, since the tears are a poor wetting agent, they do not wet the plastic contact lens. Thus, the meibomian-gland secretion is smeared onto the anterior surface of the contact lens producing a fogging of vision which is very annoying to the contact-lens wearer.

In an effort to overcome this difficulty, patients have been instructed to place their contact lenses into one of a number of wetting agents with the hope that when the lenses were inserted the tears would wet them and prevent the smearing of meibomian-gland secretion over the anterior surface of the lenses. Although these solutions were satisfactory as wetting agents, they were irritating to the conjunctiva, and patients were instructed to rinse the contact lenses well with water after removing them from the wetting agent and before inserting them. By this procedure most, if not all, of the beneficial effect of the wetting agent was lost, and the patients continued to have fogging of vision due to sebum smeared over the anterior surface of the lenses.

Therefore, a search was made to find a wetting agent which would be tolerated by the conjunctiva so that some of the wetting agent might be left in contact with the lenses, thus keeping the anterior surface of the contact lenses from becoming dry. To the author's knowledge, at the time of this writing, paratertiary-octyl-phenoxyethoxy-ethyl-dimethyl-benzyl ammonium chloride monohydrate (1:5,000) in a 2 per cent boric-acid solution is the only wetting agent that can be used without danger of producing an irritation.

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The patient is instructed that when the contact lenses are removed, they are to be placed in a small, covered jar containing an ounce or so of wetting agent. The lenses should remain in this solution until the patient is ready to reinsert them. When the lenses are taken from the jar, the excess solution should be removed by a quick shake, not by rinsing. The contact lenses are inserted in the usual manner and, after the contact lenses are in place, the eyes are washed with an eyecup filled with the wetting agent. This procedure utilizes the detergent action of the wetting agent to wash away the excess meibomian gland secretion in addition to leaving a film of wetting agent over the anterior surface of the contact lenses. This helps to keep the lenses from becoming dry and repels any remaining sebum from the anterior lens surface. (Am. J. Ophth., Aug. '47 – R. L. Schmidtke)

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Alcohol as a Disinfectant Against Mycobacterium Tuberculosis: It has been known for half a century that water is essential to the disinfectant action of ethyl alcohol, that absolute alcohol is relatively ineffective against dry bacteria, and that a final concentration of from 50 to 70 per cent appears to be optimum. For wet surfaces, from 80- to 96-percent alcohol is recommended; for dry, from 50- to 80-percent. For skin sterilization, Price showed that 70 per cent by weight is the most effective strength. Tanner and Wilson among others found that the germicidal action of aliphatic alcohols increases with the molecular weight as far as the amyl derivative (5 carbon atoms) and then decreases through octyl to undecyl alcohol (11 carbon atoms), which in action is comparable to that of ethyl. Of the water-soluble alcohols, the most effective was normal propyl.

In a review of the literature on the subject, Soberheim brought out these points: (1) Alcohol is a good disinfectant against vegetative bacteria, killing many species in from 1 to 5 minutes, but it is without effect on spores. (2) When the bacteria are in water suspension, the germicidal action of the alcohol is directly proportional to its percentage. (3) With optimum strengths of alcohol, dry bacteria are killed less easily than those in suspension. (4) Mere increase in the humidity of the room serves to increase the susceptibility of dry micro-organisms to alcohol. (5) It may be that the cell wall of the dry bacterium must absorb water and swell before alcohol can enter, and that the drying and hardening action of the higher percentage alcohols makes penetration of the inner protoplasm more difficult. (6) The coagulating action of higher percentage alcohols on albumin is hindered by their strong dehydrating effect, and this may account for the inability of such alcohols to precipitate the nucleoproteins within the unwetted cell. (7) The quantity of bacteria subjected to the action of alcohol is not of critical importance. (8) Protein, pus, and other substrates increase the disinfection time of alcohol, but not to a considerable extent. (9) The bactericidal power of alcohol is directly proportional to the temperature, and is increased by the presence of small amounts of acids, alkalis, or salts.

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In 1929 and subsequently, the action of alcohols on tubercle bacilli was investigated by Hailer. Pieces of cloth were soaked in heavy suspensions of M. tuberculosis of various strains, human and bovine. Alcohol was poured over the cloth in a dish, and at the chosen time, (2, 3, 5, 10, and 15 minutes) the action was stopped by the addition of water. Viability was proved by animal inoculation.

In these experiments Hailer found that ethyl alcohol, 50, 60, and 80 per cent by weight, killed the bacilli sometimes in 2 minutes, in most cases in 3 minutes, and always in 5 minutes. A 95-percent concentration usually killed in from 2 to 5 minutes, always in 10 minutes; and 40-percent usually in from 5 to 10, always in 15 minutes. Normal propyl alcohol, 25, 32, 40, and 48 per cent by weight, was effective, sometimes in 2 and usually in from 3 to 5 minutes; 40 and 48 per cent, always in 10 minutes; 60 per cent, always in 3 minutes. Isopropyl alcohol, 40, 48, and 60 per cent, sterilized some specimens in 2 minutes, more in 3 and 5, and most in 10 minutes; 32 per cent was always effective in 10 minutes; 48 per cent in 15 minutes.

Dealing with bits of cloth soaked in strongly positive sputum, Hailer and Heicken found that in most trials, 80- and 96-percent ethyl alcohol killed the bacilli in 5 minutes; 25- and 32-percent propyl, in 5 minutes; 40- and 48-percent isopropyl, in 10 minutes. For disinfection of the hands, Hailer and Heicken recommended immersion in the effective alcohol for 3 minutes, allowing it to dry on the hands for an additional 2 minutes. They point out that the propyl alcohols are less dangerous for hand disinfection because the lower percentages required are less inflammable. In another study Hailer found that M. tuberculosis in one-half mm. thick sputum smears, dried on pieces of wood and linoleum, were dead after 2 hours' exposure to 32-percent isopropyl alcohol. Shorter periods of exposure were not tested.

In a "tuberculocidal time-test" in which 0.5 c.c. of the reagent was incubated with 0.5 c.c. of a suspension of the bacilli, Cohn found 95-percent ethyl alcohol to be effective in a contact period of 5 minutes, but not in 2 minutes; and 20-percent alcohol, to be ineffective.

The purpose of the experiments carried out by the author was to determine the effect of alcohols in various dilutions upon dry and wet bacilli (Mycobacterium tuberculosis). Suspensions of the bacilli were made, according to a previously described method, from a virulent human strain designated as 88, the subcultures varying from 4 to 7 weeks in age. Alcohol dilutions were prepared according to directions in the United States Pharmacopoeia from Alcohol USP. Periods of exposure to the alcohols were carefully timed by stop watch, and when required, a team of several persons was used to carry out the tests in order that the timing be accurate and the details of the technic uniform. Action of the alcohols was stopped by dilution with water. All tests were made at room temperature, which varied from 20° to 22° C., with extremes of 18° and 23° C. Viability of the bacilli was tested by culture and by guinea pig inoculation.

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M. tuberculosis is remarkably sensitive to the action of alcohol; it appears to be fully as susceptible as other bacteria and subject to the same mechanism of bactericidal action. When moisture is present, the higher alcohol strengths are most effective; when absent, the middle strengths are most effective, and in the case of isopropyl alcohol, the middle and lower strengths. The presence of additional substrate in the form of sputum did not seem to diminish the disinfectant action except when the smears were increased several times in thickness. Even then the diminution was slight. Variation in the quantity of bacilli exposed to the action of alcohol showed no constant effect on the numbers surviving, although this point was not systematically investigated.

Although there were variations in technic between the different experiments, and although no attempt was made to carry out statistically significant repetitions of each test, the results were surprisingly uniform and consistent. Hailer's technic differed from this in that numbers of bacilli and amounts of sputum were probably much larger, most of his preparations were wet, and his exposure periods were not as closely timed. In general these data indicate a more rapid action, with disinfection in periods as short as 15 seconds. The conditions of these experiments were exaggerated, with the employment of larger numbers of bacilli and thicker layers of sputum than are likely to be present under ordinary conditions of contamination.

Ninety-five-percent ethyl alcohol (by volume) appears to be most active against wet tubercle bacilli; 50-percent ethyl or from 30- to 80-percent isopropyl (by weight), against dry. If one strength were to be used for all purposes, perhaps 70 per cent would be best. A critical difference between the effect of 70 per cent alcohol by volume and by weight was not shown, but these experiments were not designed to investigate this point. Isopropyl alcohol, though it was not tested against wet tubercle bacilli, appears to be at least as effective as ethyl, and in lower dilutions.

Whereas the killing time of the most effective alcohol dilutions varied from 15 seconds to between 5 and 10 minutes, the bacilli were dead in most cases at 1 or 2 minutes. Furthermore, upwards of 99 per cent of the individual bacilli did not survive the first few seconds of exposure. On this basis it may be reasonable to recommend an exposure period of from 1 to 2 minutes for some types of disinfection, and more or less than this for other types.

Isopropyl and ethyl alcohol, therefore, should be useful and practical disinfectants against the causative organisms of tuberculosis in clinics, laboratories, sanatoria, hospitals, and the home. They are relatively nonirritating, inoffensive in odor, and evaporate without leaving an annoying sediment or residuum. Their wetting properties provide a rapid spread over surfaces and promote penetration. Ethyl alcohol is fairly inexpensive for institutions that can procure it tax free. Isopropyl alcohol is reasonable in price and obtainable in all drug stores as "rubbing alcohol" in 50 or 70 per cent strengths.

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Alcohol seems particularly suitable for skin disinfection. In the case of contamination, hands may be wetted with alcohol and allowed to dry without aid, and the period of exposure will usually be 1 minute or more. Although data have not shown the change in disinfectant power due to changing alcohol percentage during evaporation, it may be expected that even with gross contamination, most or all of the bacilli would be destroyed in this period. Washing the hands with soap, followed by rinsing in 95-percent alcohol while they are wet, should be highly effective. The use of alcohol on hands or gloves between pneumothorax refills may be of distinct value in preventing cross infections. It should be useful in cleansing the area around tuberculous wounds.

Thermometers kept immersed in 70-percent alcohol (ethyl or isopropyl) should remain noninfectious if the alcohol is changed often enough to keep its strength within the effective range, perhaps once a week if well covered. Various surfaces, dishes, handicraft articles, etc., may be disinfected with alcohol if heat, sunshine, and compound solution of cresol are impractical, and if the alcohol will not be injurious. Plastics; oiled, painted, varnished, or shellacked surfaces; and some fabrics and dyes may be injured by alcohol.

As a general proposition, the use of alcohol is not recommended when less expensive disinfectants, dry or wet heat, or sunshine may be applied. It is not recommended for disinfection of masses of sputum. Grossly contaminated basins, hard surfaces, and large articles are better treated with compound cresol solution, because of its cleansing action and lower cost.

Alcohol must be used with caution on instruments such as cystoscopes and thoracoscopes containing lens systems that may be held in position with alcohol-soluble cement. (Pub. Health Reps., 5 Sept. '47 - C. R. Smith)

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Preliminary Report on Some Organic Materials as Repellents and Toxic Agents for Ticks: During the past year some 80 organic materials have been appraised at the Rocky Mountain Laboratory in search of an effective agent for the protection of man from ticks. This paper briefly summarizes an evaluation of 15 of these materials, both for repellency and acaricidal properties. Details of experiments and complete test data will be presented in a subsequent report.

Tests as Repellents. The criterion for evaluating repellency was the number of ticks observed on untreated socks as compared with treated ones. The latter were impregnated at the rate of two milliliters (liquid) or grams (solid) per square foot. Socks were worn by subjects exposed for 15 minutes to several thousand ticks under simulated natural conditions. Adults and nymphs of the lone star tick (Amblyomma americanum) and adults of the Rocky Mountain wood tick (Dermacentor andersoni) were used in these tests. In order to determine the persistence of effectiveness following treatment of the socks, observations were made over a period of 4 weeks, but no tests were made during the third week following treatment.

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The materials reported on are:

Dibenzyl
2-Phenyl cyclohexanol (Tech.)
6-2-2 Mixture (60% Dimethyl phthalate, 20% Indalone, 20% Rutgers 612)
p-n-Propoxybenzaldehyde
Phthalic acid, hexahydro, diethyl ester
iso-Propyl cinnamate
N-Ethylacetanilide
Dibutyl phthalate
Dimethyl phthalate
1-Benzyl cyclohexanol-1
2-Propyl-5-methyl-5-nitro-m-dioxane
Benzyl benzoate
N-n-Butylacetanilide
N-n-Propylacetanilide
Ethyl cyclohexylcyanoacetate

All these materials gave some degree of protection, and generally were much more effective against A. americanum than against D. andersoni.

Little protection against D. andersoni was afforded by dibenzyl, benzyl benzoate, dimethyl phthalate, and 2-propyl-5-methyl-5-nitro-m-dioxane and somewhat more, but still insufficient, protection by 6-2-2 mixture, ethylacetanilide and dibutyl phthalate. Butylacetanilide, ethyl cyclohexylcyanoacetate, phenyl cyclohexanol, benzyl cyclohexanol, and phthalic acid, hexahydro, diethyl ester gave upwards from 90 per cent protection against D. andersoni through 2 weeks after treatment, but, with the exception of butylacetanilide, showed a considerable reduction in effectiveness after the fourth week. Ethyl cyclohexylcyanoacetate gave complete protection when freshly applied, as did butylacetanilide the second week after treatment.

All materials, except dibenzyl, iso-propyl cinnamate, and ethylacetanilide gave from 95 to 100 per cent protection against A. americanum adults throughout 4 weeks following treatment. Although these three gave more than 95 per cent protection through 2 weeks following treatment, they gave less than 90 per cent protection after 4 weeks. Phenyl cyclohexanol, benzyl cyclohexanol, dimethyl phthalate, and propylacetanilide gave complete protection from A. americanum adults throughout the entire series of tests, and butylacetanilide, ethyl cyclohexylcyanoacetate, benzyl benzoate, dibutyl phthalate, 6-2-2, and propoxybenzaldehyde gave from 99 to 100 per cent protection.

Although none of the materials gave complete protection from A. americanum nymphs throughout the entire series of tests, the results were consistent with and quite similar to those recorded for the adults, and in general all materials gave a persistently high degree of protection.

Effect of Rinsing. The effectiveness of the majority of the materials tested for repellency was completely lost or greatly reduced as a result of rinsing the

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treated socks in warm tap water. Dibutyl phthalate, phenyl cyclohexanol, benzyl benzoate, and butylacetanilide continued to give adequate protection from A. americanum, but not from D. andersoni.

Tests as Acaricides. These same materials were tested for toxicity against larvae, nymphs, and adults of D. andersoni by confining them to squares of cloth impregnated at the rate of four milliliters (liquid) or grams (solid) per square foot, and observing the average time required for their immobilization.

None of the materials stopped adults within a 2-hour exposure period.

Phenyl cyclohexanol, propoxybenzaldehyde, and benzyl cyclohexanol stopped larvae in less than 15 minutes. Butylacetanilide, propylacetanilide, ethylacetanilide, iso-propyl cinnamate, and phthalic acid, hexahydro, diethyl ester stopped larvae in less than 30 minutes, but more than 15 minutes. Benzyl benzoate, 2-propyl-5-methyl-5-nitro-m-dioxane, dimethyl phthalate, and the 6-2-2 mixture stopped larvae in less than 60 minutes, but more than 30 minutes. Dibenzyl, dibutyl phthalate, and ethyl cyclohexylcyanoacetate failed to stop larvae within a 2-hour observation period.

Nymphs were immobilized by phenyl cyclohexanol in 34 minutes, by ethyl-acetanilide in 23 minutes, by propylacetanilide in 58 minutes, and by phthalic acid, hexahydro, diethyl ester in 2 hours. Butylacetanilide, 6-2-2, and benzyl cyclohexanol greatly enfeebled nymphs in less than 45 minutes, but did not stop them within 2 hours. Ethyl cyclohexylcyanoacetate, propoxybenzaldehyde, and iso-propyl cinnamate had little effect on nymphs, and dimethyl phthalate, dibenzyl, 2-propyl-5-methyl-5-nitro-m-dioxane, benzyl benzoate, and dibutyl phthalate appeared to be wholly ineffective.

Some Observations on the Practical Application of Repellents. In the course of the routine collecting last spring of D. andersoni adults by seven members of the Laboratory personnel, it was possible to make limited tests with two com-pounds, 2-phenyl cyclohexanol and dibutyl phthalate, under field conditions. White coveralls are regularly worn by persons so employed. Observations were irregular, and only incomplete data were obtained because of frequent unfavora-ble weather conditions.

Some coveralls and socks were impregnated with 2 ounces of the materials, others were untreated. Repellency was evaluated by the percentage of reduction in the number of ticks on treated clothing below the number on untreated clothing during a day.

Dibutyl phthalate was 87 per cent effective 1 day after treatment, 78 per cent effective on the fourth day, 87 per cent effective on the tenth day, and 84 per cent effective on the twelfth day. Phenyl cyclohexanol was 92 per cent effective 1 day after treatment and 100 per cent effective on the fourth day.

These results are consistent with those obtained from the tests of repellents under simulated field conditions.

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Discussion. It is apparent from the results of all tests that none of the materials reported on can be entirely disregarded as an agent of some potential value for protecting man against ticks. None of them stains fabrics. The odors of iso-propyl cinnamate, propoxybenzaldehyde, ethylacetanilide, and propylacet- anilide were objectionable to a majority of 20 persons. Tests by others, includ- ing the United States Food and Drug Administration, have demonstrated that phenyl cyclohexanol, benzyl benzoate, dibutyl phthalate, 6-2-2, propoxybenzalde- hyde, ethylacetanilide, propylacetanilide, ethyl cyclohexylcyanoacetate, dimethyl phthalate, and 2-propyl-5-methyl-5-nitro-m-dioxane can be used safely from the standpoint of irritation to the skin. Data relative to the possible toxicity and ir- ritation to man of the other compounds were not available to the writer.

Although the data are not extensive enough to be conclusive, a comparison of the results from all tests strongly suggests that phenyl cyclohexanol and butylacetanilide are very promising agents against Dermacentor andersoni and Amblyomma americanum. (Pub. Health Reps., 8 Aug. '47 - J. M. Brennan)

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Smallpox Immunization Requirements for Persons Entering the United States from Europe: Europe is now among the areas from which introduction of smallpox into the United States is considered a threat. Persons arriving from Europe are now required to present a certificate showing that they have been successfully vaccinated against smallpox within the last three years, or show physical evidence that they have had smallpox.

Travelers who cannot prove immunity to smallpox must either consent to an immediate vaccination or remain under observation of quarantine officials until the incubation period for the disease is passed. This period will not ex- ceed 14 days after arrival.

Increased air travel, which results in travelers reaching the United States before outbreaks of smallpox in foreign countries can be reported to quarantine officials, necessitated the new immunization requirement, according to United States Public Health Service officials who announced the new requirements on 13 August 1947.

As a further protection, arrangements are being made with the transporta- tion industry to refuse to sell tickets to persons who cannot show proof of small- pox immunity. Until this ruling becomes effective, quarantine officers of the United States Public Health Service will continue to enforce the program of vac- cinating or detaining all nonimmune persons. (Pub. Health Reps. 29 Aug. '47)

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REVISED AUTHORIZED BED CAPACITIES OF U. S. NAVAL HOSPITALS FOR 2nd QUARTER OF FISCAL YEAR 1948

CONTINENTAL NAVAL HOSPITALS

			2nd Quarter
1st	ND -	NH, Chelsea, Mass.	700
		NH, Newport, R.I.	750
		NH, Portsmouth, N.H.	150
3rd	ND -	NH, Brooklyn, N.Y.*	300
		NH, St. Albans, N.Y.	1550
4th	ND -	NH, Philadelphia, Pa.	1250
SRNC	-	NH, Annapolis, Md.	200
PRNC	-	NH, NNMC, Bethesda, Md.	1300
		NH, Quantico, Va.	150
5th	ND -	NH, New River, N.C. (Camp Lejeune)	300
		NH, Portsmouth, Va.	1200
6th	ND -	NH, Charleston, S.C.	450
		NH, Dublin, Ga.	400
		NH, Parris Island, S.C.	150
7th	ND -	NH, Jacksonville, Fla.	550
		NH, Key West, Fla.	150
8th	ND -	NH, Corpus Christi, Texas	400
		NH, Houston, Texas	470
		NH, Memphis, Tenn.	250
		NH, Pensacola, Fla.	350
		Naval Unit, USPH Hosp., Ft. Worth, Texas	400
9th	ND -	NH, Great Lakes, Ill.	900
11th	ND -	NH, Corona, Calif.	700
		NH, Long Beach, Calif.	1350
		NH, San Diego, Calif.	1500
		NH, Santa Margarita Ranch, Calif.	300
12th	ND -	NH, Mare Island, Calif.	800
		NH, Oakland, Calif.	1750
13th	ND -	NH, Puget Sound, Bremerton, Wash.	600
		SUB TOTAL	19,320

EXTRACONTINENTAL NAVAL HOSPITALS

NH, Aiea Heights, Pearl Harbor, T. H.	750
NH, Coco Solo, C. Z.	150
NH, Guam, M. I.	500
NH, Guantanamo Bay	150
SUB TOTAL	1,550
GRAND TOTAL	20,870

*Brooklyn Hospital to be disestablished when suitable facilities become available at St. Albans for treatment and care of cancer patients and naval dependents.

H. L. Pugh, Acting Chief of Bureau

(Not Restricted)

Postgraduate Courses at Naval Dental School: Dental officers of the ranks
as listed completed on 3 October 1947, the following postgraduate courses
given at the U. S. Naval Dental School, National Naval Medical Center,
Bethesda, Maryland:

General Postgraduate Course

    8 Commanders
    1 Lieutenant Commander
    1 Lieutenant (j.g.)

Specialized Course in Oral Surgery

    1 Commander
    1 Lieutenant Commander
    1 Lieutenant

Specialized Course in Prosthodontia

    3 Commanders

All assignments to the next classes in the above courses, scheduled to be-
gin on 13 October 1947, have been made and will include 4 dental officers from
countries in South America. (Dental Div., BuMed)

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Downgrading of Issue of Bumed News Letter: By action of the Chief of
BuMed, the issue of the Bumed News Letter of 18 August 1944 has been down-
graded from "Restricted" to "Not Restricted."

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(Not Restricted)

Personnel of the Medical Department Requested to Aid in the Recruit-
ment and Reenlistment of Hospital Corpsmen: The records of the Bureau of
Medicine and Surgery indicate that the enlistments of some 10,800 Hospital
Corpsmen will expire during the fiscal year. It is estimated that approxi-
mately 1,200 men will be lost from the Service due to special order, physical
disability, and miscellaneous discharges. In order to maintain the Hospital
Corps at the allowed enlisted strength for the Fiscal Year 1948, approximately
6,000 men will have to be procured either from reenlistments or from initial
recruitment.

The Surgeon General has noted, with gratification, the efforts of Medical
Department personnel in effecting a noticeable increase recently in the Hospi-
tal Corps reenlistment rate. The average percentage for July and August has
been 51 per cent, as compared with a monthly average of approximately 30 per
cent previously.

(Not Restricted)

For every trained Hospital Corpsman who reenlists the government is saved the expense, effort, and time consumed in the recruitment and training of one new man. Therefore, it is urgently requested that the commendable efforts recently expended in bringing to the attention of members of the Hospital Corps the many advantages of continuous service in the Navy - the benefit of early retirement with substantial pay, an honorable career with steady advancement to all those who apply themselves, allowances and medical care for dependents, the opportunity for selection to officer status, - be continued with a view toward obtaining as high a percentage of reenlistments as possible.

The following references concern enlistments and recruitments:

> AlNav 134-47 (Enlistment terms reduced).
> AlNav 147-47 (Early discharge for reenlistment authorized).
> BuPers C/L 102-47 (Extension of enlistment terms reduced).
> BuPers C/L 141-47 (Reenlistment on any ship or station authorized).

(H. L. Pugh, Acting Chief of Bureau)

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(Not Restricted)

<u>Dental Service of Philadelphia Naval Hospital Approved</u>: The Executive Committee of the Hospital Dental Service Committee of the American Dental Association on 24 June 1947 approved the dental service of the U. S. Naval Hospital, Philadelphia, Pennsylvania.

Continuation of the approval is contingent upon maintenance of the basic standards for hospital dental service as established or amended by the Hospital Dental Service Committee of the American Dental Association. (Dental Div., BuMed)

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(Not Restricted)

<u>Receipt of Patients in Naval Hospitals without Records and Baggage</u>: The report below was recently received in the Bureau of Medicine and Surgery. Because it concerns a matter of interest and importance, it is brought to the attention of all Medical Department personnel for information and guidance. It is desired that all necessary steps be taken to insure full compliance with existing directives (including BuPers Circular Letter 100-44, N. D. Bulletin, Cumulative Edition, Jan.-June, 1944, page 522) having to do with the subject matter of this report.

> "Refs: (a) Article D-7010, BuPers Manual.
>   (b) Article D-7011, BuPers Manual.
>   (c) Article 1804, U. S. Navy Regulations.
>   (d) BuPers C/L 148-42, Pers-618-MSM, P20-2(43) of
>   27 Oct 1942.
>   (e) Para. 219, NavPers 15, 642.

(Not Restricted)

1. The following facts, substantiated by a recent survey by this hospital, are submitted to the Bureau for review, consideration, and possible corrective measures:

(a) Subsequent to the institution of the current Navy Personnel Accounting System, this hospital has experienced extreme difficulty in obtaining records and accounts of patients received for treatment from activities and ships in this vicinity. The hospital files reveal that during the month of June 1947, 697 of enlisted personnel were admitted for treatment. Of this number, 125 (18 per cent) were accompanied by proper records. Only 256 (37 per cent) were received with the service records. Four hundred and eighty-five (69 per cent) were received with the health record, and 495 (71 per cent) were received with NavMed Form-G. One hundred and ninety-seven (29 per cent) were admitted accompanied by their personal effects as required by reference (b). Two hundred and eighteen (31 per cent) were admitted with pay accounts. Thirty-five (5 per cent) were admitted and discharged before receipt of the service record. Forty-eight (7 per cent) were emergency admissions, admitted direct for treatment. In these latter cases, this hospital is aware that records and effects must follow at a later date upon proper notification of admission to the command concerned.

(b) Roughly 30 per cent of the records and accounts are received from two to three weeks after admission, and in numerous cases after the patient has been discharged from treatment and returned to his duty station. When the service record arrives two or three days before the date on which the patient is ready for discharge from treatment, it is impossible to clear the record through personnel accounting in time to accompany the patient when he is transferred to duty.

(c) Failure of the commands concerned to comply with existing directives outlining proper procedure to follow in the transfer of records with the patient necessitates duplication of various administrative procedures. For example, the completion of NavPers 500 and 501 (the most important phase of the administrative work connected directly with the Personnel Accounting System of the Navy) in accordance with reference (e), requires the personnel officer so assigned to certify all entries listed therein. The service record and the number three NavPers 500 card are required to effect this certification. In the absence of the service record, a skeleton NavPers 500 card must be submitted on admission of the patient and this card must be supplemented by a complete and correct card subsequent to receipt of the service record.

(d) Over 40 per cent of the pay accounts of patients received for treatment are received from two to three weeks after admission. Not only does this delay proper administrative work on the patient, but it also creates a hardship from a monetary point of view. This delinquency frequently necessitates that temporary pay accounts be prepared on the man concerned in accordance with reference (c).

(Not Restricted)

(e) In some cases, the patient arrives in a serious or critical condition. In these cases, the address of the next of kin should be obtained from the service record in order that the person concerned may be informed of the patient's condition. Since the health record does not reveal a sworn statement certifying the address of the next of kin, it is the policy of this command to verify this from the service record. In the absence of the service record, great difficulty is involved in ascertaining the correct address.

(f) Numerous activities have communicated telephonically with this command and questioned the reason why they were receiving numerous requests to forward the proper records of patients admitted from their activity. It is obvious that these commands have not instituted measures for the proper indoctrination of the personnel delegated the duties of transferring personnel to hospitals or elsewhere. From their questions, it is apparent that they have not reviewed the Bureau's instructions or Navy Regulations pertaining to the administration of personnel and the records thereof, which, in all cases, concisely and definitely outline the correct procedure.

(g) There are other instances in which only service record pages 9y are received from activities and ships and these have on them the statement that the service record and pay account are being retained by the transferring command. This is in direct contradiction with references (a) and (d).

2. It is realized that the Navy is now completing transformation from war to peace and that there exists a critical shortage of trained and competent personnel. Nevertheless, officers vested with the authority to transfer personnel should receive definite instructions to review pertinent directives and to establish an organization and functions in accordance with the policy and regulations of the Navy."

It is desired that Medical Department personnel concerned take all necessary steps to insure compliance with the existing directives concerning the subject matter of this report. (H. L. Pugh, Acting Chief of BuMed)

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ALNAV 209   29 September 1947   (Not Restricted)

Subj: Cholera Immunization

Reference Manual Medical Department, Paragraph 35B24.1. Until further notice all persons traveling under cognizance of Navy Department shall be immunized against cholera prior to embarkation for Egypt.   --SecNav.

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JOINT LETTER

Circular Letter 47-123   9 September 1947   (Not Restricted)

To: All Ships and Stations

Subj: Casualty Reporting Procedure and Release of Casualty Information for
       Publication

Refs: (a) Alnav 13-42
       (b) Alnav 162-42
       (c) Alnav 258-42
       (d) Alnav 48-45
       (e) Alnav 58-45
       (f) Alnav 120-45
       (g) Alnav 80-46
       (h) Alnav 301-46

1. This letter supersedes the above references, which are hereby canceled.

2. Effective upon receipt of this letter the procedure for reporting casualties
will be in accordance with Articles 908 and 1513 Navy Regulations, Articles
C-7002, D-9601 and H-1905 (H-1906, Part H, Revised 1947, distribution of which
is not completed) Bureau of Naval Personnel Manual; paragraphs 341, 3417,
3418, 3419 and 16A9.2 Manual of the Medical Department, United States Navy;
and Articles 1-22 and 3-1 to 3-4 Marine Corps Manual. Persons missing under
circumstances not indicative of voluntary absence will be similarly reported.
When evidence is conclusive that a missing person is dead submit a report of
death with such appropriate remarks as "body not recovered" or "not identi-
fied" In all cases of serious injury or illness Commanding Officers outside
the continental United States having medical custody will submit by dispatch to
the Bureau of Naval Personnel or the Commandant of the Marine Corps an origi-
nal report on admission, including sufficient information for notifying the next
of kin and will follow with prognosis and progress reports as conditions change
until the patient is removed from the serious list.

3. Names of casualties will not be released for publication prior to a lapse of
four hours after release of the notification telegram to the next of kin. In cases
of multiple casualties, when notification to the next of kin of all persons involved
will be delayed due to lack of information or identification of some individuals,
partial release of the names of casualties to the press will not be made without
the prior approval of the Bureau of Naval Personnel or the Commandant of the
Marine Corps.

4. Responsibility for notification of the next of kin and control of release to the
press within the continental United States will be upon the Commanding Officer
and/or the Commandant of the Naval District or River Command within which
the casualty occurred, except when the next of kin resides outside the United

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States. If unable to notify the next of kin promptly, the responsible command will notify the Secretary of the Navy by dispatch with the Bureau of Naval Personnel or the Commandant of the Marine Corps as information addressees, giving the reason the next of kin cannot be notified and furnishing complete information as required by Article 908 Navy Regulations.

5. Responsibility for the notification of the next of kin of casualties occurring outside the continental United States, or when death occurs within the United States and the next of kin resides outside the United States, will rest with the Bureau of Naval Personnel or the Commandant of the Marine Corps. Commands beyond the continental United States are authorized to release casualty information to the press four hours after release of the notification dispatch to the next of kin. For beginning of the four hour interval commands outside the continental United States are directed to use the date-time group of the dispatch which the Bureau of Naval Personnel or the Commandant of the Marine Corps will send to these commands stating that the next of kin have been notified.

T. L. Sprague   A. A. Vandegrift   C. A. Swanson
Chief, BuPers   Comdt, MarCorps   Chief, BuMed

Approved:

James Forrestal
Secretary of the Navy

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Circular Letter 47-130   18 September 1947   (Not Restricted)

To: All Ships and Stations

Subj: Diathermy Apparatus, Short Wave, 110 Volt, 60 Cycle, A. C.; limitation of use

Ref: (a) Federal Communications Commission Rules and Regulations (Title 47-Telecommunication - Chapter I) Part 18, Rules and Regulations Relating to Industrial, Scientific and Medical Service. (Effective June 15, 1947.)

1. In accordance with a recent ruling of the Federal Communications Commission, medical diathermy equipment procured prior to 1 July 1947 cannot be used after 30 June 1952. Therefore, on each short wave diathermy apparatus in use or in storage, upon receipt of this letter, there shall be permanently attached a label which reads as follows:

"In accordance with Federal Communications Commission Rules and Regulations (Title 47-Telecommunication Chapter I), Part 18, Rules

(Not Restricted)

and Regulations Relating to Industrial, Scientific and Medical Service, Effective 15 June 1947, this equipment shall not be used after 30 June 1952."

2. The above mentioned requirement is applicable to any short wave diathermy apparatus on hand or in use, at the present time, standard or nonstandard, regardless of whether or not the unit operates within the presently assigned frequency.

3. Future procurement of short wave diathermy apparatus will specify delivery with a dated name plate and indication of Federal Communications Commission's type approval and, therefore, will not require the above label.

--BuMed.   H. L. Pugh

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Circular Letter 47-131   22 September 1947   (Not Restricted)

To: Medical Officers in Command, All Naval Hospitals

Subj: Cross-Index System for Clinical Records

Ref: (a) NAVMED 1193 - Cross-Index System for Clinical Records for
            Use in Naval Hospitals.

1. Instructions contained in ref. (a) required the medical records librarian to submit to the Medical Officer in Command a quarterly summary of the hospital's experience as reflected by the cross index. A copy of this quarterly report shall be submitted to the Bureau. The initial report should be for the quarter ending 30 September 1947, covering such portion of the quarter as the cross index system has been in operation.

--BuMed.   H. L. Pugh

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